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CLAIMS

1. A controlled release dosage form comprising:

(a) a core comprising an osmotic agent and a low solubility drug in the form of a solid dispersion of said drug in a dispersion polymer, at least a major portion of said drug being amorphous; and

(b) a substantially water-permeable coating around said core having at least one delivery port therein, said coating controlling the influx of water to said core from an aqueous environment of use so as to cause extrusion of at least a portion of said core through said at least one delivery port to said aqueous environment of use, said coating being non-dissolving and non-eroding during release of said drug.

2. The dosage form of claim 1 wherein substantially all of said drug is amorphous.

3. The dosage form of claim 1 wherein essentially all of said drug is amorphous.

4. The dosage form of claim 1 wherein said coating is a polymeric membrane.

5. The dosage form of claim 4 wherein said polymeric membrane is semipermeable.

6. The dosage form of claim 4 wherein said polymeric membrane is porous.

7. The dosage form of claim 4 wherein said polymeric membrane comprises at least one asymmetric membrane.

8. The dosage form of claim 7 wherein said at least one delivery port comprises pores in said coating.

9. The dosage form of claim 1 wherein said at least one delivery port is formed by laser drilling.

10. The dosage form of claim 1 wherein said at least one delivery port is formed in said environment of use.

11. The dosage form of claim 10 wherein said at least one delivery port is formed by the erosion of a plug of water-soluble material.

12. The dosage form of claim 10 wherein said coating is rupturable to form said at least one delivery port.

13. The dosage form of claim 12 wherein said at least one delivery port is formed by a rupture of a relatively small portion of said coating.

14. The dosage form of claim 13 wherein said rupture takes place in a thinner portion of said coating over an indentation in said core.

15. The dosage form of claim 4 wherein said coating is formed from a polymer selected from the group consisting of poly(acrylic) acids and esters; poly(methacrylic) acids and esters; copolymers of poly(acrylic) and poly(methacrylic) acids and esters; cellulose esters; cellulose ethers; and cellulose ester/ethers.

16. The dosage form of claim 4 wherein said coating is formed from a polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, copolymers of polyethylene glycol and polypropylene glycol, poly(vinylpyrrolidone), ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, carboxymethylethyl cellulose, starch, dextran, dextrin, chitosan, collagen, gelatin, bromelain, cellulose acetate, unplasticized cellulose acetate, plasticized cellulose acetate, reinforced cellulose acetate, cellulose acetate phthalate, cellulose acetate trimellitate, hydroxypropylmethylcellulose, hydroxypropylmethyl-cellulose phthalate, hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose acetate trimellitate, cellulose nitrate, cellulose diacetate, cellulose triacetate, agar acetate, amylose triacetate, beta glucan acetate, beta glucan triacetate, acetaldehyde dimethyl acetate, cellulose acetate ethyl carbamate, cellulose acetate phthalate, cellulose acetate methyl carbamate, cellulose acetate succinate, cellulose acetate dimethaminoacetate, cellulose acetate ethyl carbonate, cellulose acetate chloroacetate, cellulose acetate ethyl oxalate, cellulose acetate methyl sulfonate, cellulose acetate butyl sulfonate, cellulose acetate propionate, cellulose acetate p-toluene sulfonate, triacetate of locust gum bean, cellulose acetate with acetylated hydroxyethyl cellulose, hydroxlated ethylene-vinylacetate, cellulose acetate butyrate, polyalkenes, polyethers, polysulfones, polyethersulfones, polystyrenes, polyvinyl halides, polyvinyl esters and ethers, natural waxes and synthetic waxes.

17. The dosage form of claim 1 in a form selected from the group consisting of a tablet, a capsule a bead and a collection of at least two types of beads

having different drug release properties, and wherein the environment of use is a human gastrointestinal tract.

18. The dosage form of claim 1 wherein said osmotic agent is selected from the group consisting of an osmotically effective solute and a water-swellable hydrophilic polymer

19. The dosage form of claim 18 wherein said osmotic agent is water-swellable and substantially segregated from said solid dispersion.

20. The dosage form of claim 19 wherein said osmotic agent and said solid dispersion are in respective discrete layers.

21. The dosage form of claim 20 wherein said osmotic agent is in a first layer and said solid dispersion is in a second layer.

22. The dosage form of claim 21, including solid dispersion in a third layer wherein said osmotic agent is between said first layer and said second layer.

23. The dosage form of claim 19 wherein said solid dispersion surrounds said osmotic agent.

24. The dosage form of claim 1 wherein said osmotic agent and said dispersion polymer are the same.

25. The dosage form of claim 18 wherein said water-swellable hydrophilic polymer is selected from the group consisting of hydrophilic vinyl and acrylic polymers, polysaccharide alginates, poly(ethylene oxide), polyethylene glycol, polypropylene glycol, poly(2-hydroxyethyl methacrylate), poly(acrylic) acid, poly(methacrylic) acid, polyvinyl pyrrolidone,

crosslinked polyvinyl pyrrolidone, polyvinyl alcohol, polyvinyl pyrrolidone/polyvinyl alcohol copolymers, vinyl acetate, hydrophilic polyurethanes containing large polyethylene oxide blocks, carrageenan, hydroxethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose, carboxyethylcellulose, sodium alginate, polycarbophil, gelatin, xanthan gum, sodium croscarmellose, and sodium starch glycolate.

26. The dosage form of claim 25 wherein said water-swellable hydrophilic polymer is selected from the group consisting of polyethylene oxide, polyethylene glycol, carboxymethylcellulose, polyvinyl pyrrolidone, hydroxypropylmethylcellulose, poly(acrylic) acid, crosslinked poly(acrylic) acid, sodium croscarmellose and sodium starch glycolate.

27. The dosage form of claim 1 wherein said core further comprises a solubility-enhancing agent.

28. The dosage form of claim 27 wherein said solubility-enhancing agent is selected from the group consisting of organic acids and organic acid salts; partial glycerides; glycerides; glyceride derivatives; polyethylene glycol esters; polypropylene glycol esters; polyhydric alcohol esters; polyoxyethylene ethers; sorbitan esters; polyoxyethylene sorbitan esters; carbonate salts; and cyclodextrins.

29. The dosage form of claim 1 wherein said solid dispersion is formed by spray-drying.

30. The dosage form of claim 1 wherein said dispersion polymer is selected from the group consisting of:

(a) ionizable cellulosic polymers;

(b) nonionizable cellulosic polymers; and

(c) vinyl polymers and copolymers having substituents selected from the group consisting of hydroxyl, alkylacyloxy and cyclicamido.

31. The dosage form of claim 30 wherein said dispersion polymer comprises hydroxypropylmethyl-cellulose, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose acetate phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl pyrrolidone, polyvinyl alcohol, and copolymers of polyvinyl pyrrolidone and polyvinyl alcohol.

32. The dosage form of claim 29 wherein, prior to formation of said solid dispersion, said drug is amorphous.

33. The dosage form of claim 29 wherein, prior to formation of said solid dispersion, said drug is crystalline.

34. The dosage form of claim 1 wherein said core further comprises excipients.

35. The dosage form of claim 34 wherein said excipients are selected from the group consisting of surfactants, water-soluble polymers, pH modifiers, fillers, binders, pigments, lubricants, antioxidants and flavorants.

36. The dosage form of claim 1 wherein said dosage form provides a maximum concentration of said drug in a use environment that is at least 1.2-fold that of a control dosage form comprising an identical dosage form containing an equivalent quantity of undispersed drug.

37. The dosage form of claim 1 wherein said dosage form provides an AUC in a use environment that is at least 1.25-fold that of a control dosage form comprising an identical dosage form containing an equivalent quantity of undispersed drug.

38. The dosage form of claim 1 wherein said dosage form is dosed orally to a mammal, said dosage form provides an AUC in drug concentration in the blood that is at least 1.25-fold that of a control dosage form comprising an identical dosage form except containing an equivalent quantity of undispersed drug.

39. The dosage form of claim 38 wherein said dosage form provides a maximum drug concentration in the blood at a t_{max} which is at least 30 minutes longer but not more than 24 hours longer than the t_{max} observed for said control dosage form.

40. The dosage form of claim 1 wherein said drug is selected from the group consisting of an anti-hypertensive, and antianxiety agent, an anticlotting agent, a blood glucose-lowering agent, a decongestant, an antihistamine, an antitussive, an anti-inflammatory, an anti-atherosclerotic agent, an antipsychotic agent, a cognitive enhancer, a cholesterol-reducing agent, an antiobesity agent, an autoimmune disorders agent, a hypnotic agent, an anti-Parkinsonism agent, an antibiotic, an antiviral agent, an anti-impotence agent, an anti-neoplastic, a sedative, a barbituate, a nutritional agent, a beta-blocker, an emetic, an anti-emetic, a diuretic, an anticoagulant, a cardiotonic, an androgen, a corticoid, an anabolic agent, an anti-depression agent, an anti-infective agent, a coronary vasodilator, a carbonic anhydrase inhibitor, an antifungal, an antiprotozoal, a gastrointestinal agent, a dopaminergic agent, an anti-Alzheimer's Disease agent, an

anti-ulcer agent, a platelet inhibitor, and a glycogen phosphorylase inhibitor.

41. The dosage form of claim 40 wherein said drug is an antihypertensive selected from the group consisting of prazosin, nifedipine, trimazosin and doxazosin.

42. The dosage form of claim 40 wherein said drug is the antipsychotic agent ziprasidone.

43. The dosage form of claim 40 wherein said drug is the blood glucose-lowering agent glipizide.

44. The dosage form of claim 40 wherein said drug is an anti-impotence agent selected from the group consisting of sildenafil and pharmaceutically acceptable salts thereof.

45. The dosage form of claim 40 wherein said drug is the anti-inflammatory agent (+)-N-{4-[3-(4-fluorophenoxy)phenoxy]-2-cyclopenten-1-yl}-N-hyroxyurea.

46. The dosage form of claim 40 wherein said drug is an antidepression agent selected from the group consisting of fluoxetine, paroxetine, venlafaxine, sertraline, [3,6-Dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethylpropyl)-amine and 3,5-dimethyl-4-(3'-pentoxy)-2-(2',4',6'-trimethylphenoxy)pyridine.

47. The dosage form of claim 40 wherein said drug is a glycogen phosphorylase inhibitor selected from the group consisting of [R-(R*S*)]-5-chloro-N-[2-hydroxy-3-[methoxymethylamino}-3-oxo-1-(phenylmethyl)propyl]propyl]-1H-indole-2-carboxamide and 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzl;-

3((3R,4S)-dihydroxypyrrolidin-1-yl-)-(2R)-hydroxy-3-oxypropyl]amide.

48. A method of treating a disease or disorder in a person comprising administering to said person a dosage form comprising:

(a) a core comprising an osmotic agent and a low solubility drug in the form of a solid dispersion of said drug in a dispersion polymer, at least a major portion of said drug being amorphous polymer; and

(b) a substantially water-permeable coating around said core having at least one delivery port therein, said coating controlling the influx of water to said core from an aqueous environment of use so as to cause extrusion of at least a portion of said core through said at least one delivery port to said aqueous environment of use, said coating being non-dissolving and non-eroding during release of said drug.